

EFFECT OF LABETALOL AND ESMOLOL ON ONSET OF ACTION OF ROCURONIUM: A PROSPECTIVE DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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Received: 05 January 2018, Revised and Accepted: 19 February 2018

ABSTRACT

Objective: Labetalol is a non-selective beta blocker which is used for the treatment of hypertension. Its role in controlling the hemodynamic response to tracheal intubation is established. This comparative controlled study was carried out to verify its effects on time to onset of action of rocuronium in comparison to esmolol.

Methods: We randomized patients into two groups. Group A receiving injection labetalol 0.25 mg/kg diluted to 10 ml with 0.9% saline and Group B receiving 0.5 mg/kg of esmolol in 10 ml 0.9% saline before surgery. The time to onset of action of rocuronium, systolic blood pressure, and heart rate were recorded. The adverse reactions were observed in the post-operative period.

Results: A total of 60 patients were randomized into two groups. At the time of intubation, the systolic blood pressure and heart rate were similar between the two groups. The onset of action of rocuronium was decreased significantly in the labetalol group.

Conclusion: Labetalol attenuates the hemodynamic response to tracheal intubation both during intubation. It also slightly decreases the time to onset of action of rocuronium.

Keywords: Rocuronium, Muscle relaxation, Labetalol.

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INTRODUCTION

Endotracheal intubation is the gold standard method for maintaining the airway during general anesthesia. Direct laryngoscopy and passage of a tracheal tube are noxious stimuli that can provoke adverse responses in cardiovascular, respiratory, and other physiological systems. Significant tachycardia and hypertension [1] are associated with intubation. The elevation in arterial pressure typically starts within 5 s of laryngoscopy, peaks in 1–2 min, and returns to control levels within 5 min. Such hemodynamic changes can result in myocardial ischemia by increasing the myocardial oxygen requirement but seem to cause little harm to most patients. However, they are undesirable in patients with the coexisting cardiac disease.

Various drugs have been used to blunt this hemodynamic response such as β blockers [2], α_2 agonist [3], local anesthetics [4], and opioids [5]. Among the narcotics fentanyl, 6 μ g/kg suppresses the hemodynamic response but risks prolonged respiratory depression. Among the β blockers, the most commonly used is esmolol. Esmolol [6] is a selective β_1 receptor blocker with a very short duration of action. Esmolol because of its selective action decreases the cardiac output. This decrease in cardiac output increases the time to onset of action of rocuronium. Rocuronium [6] is an intermittently acting muscle relaxant. Its advantage is its quick onset of action which is comparable with succinylcholine. This advantage gets a little delayed due to the use of esmolol. Labetalol is a non-selective β blocker [7] with additional α_1 antagonistic property. It is primarily used for the treatment of hypertension. Labetalol due to its peripheral vasodilation property does not affect the cardiac output [8]. Labetalol has been shown to have an effect on blunting the hemodynamic response to tracheal intubation [9-11]. Thus, we hypothesized that labetalol while blunting the hemodynamic response to tracheal intubation will not lengthen the time to onset of action of rocuronium. Therefore, a prospective randomized, double-blind study was conducted on patients posted for mastoidectomy in the ear, nose, and throat (ENT) OT.

METHODS

After the study was approved by the Ethics Committee of the Institute of Medical Sciences (IMS) and SUM Hospital, we obtained a well-informed consent of 60 patients scheduled for mastoidectomy surgery. The study period lasted for 14 months starting from August 2015. The exclusion criteria were atherosclerosis, diabetes mellitus, asthma, hypertensive, any cardiac disorder, hemodynamically instability, hypersensitivity to the study drugs, Mallampatti Grade III/IV, and body mass index (BMI) more than 30. The randomization was done using a computer generated random number table. Each consenting patient received a consecutive randomization number.

The patients were explained the procedure and the drugs used during the pre-anesthetic evaluation. Overnight anxiety was prevented by giving alprazolam 0.25 mg tablet at bedtime along with one tablet of ranitidine 300 mg to decrease gastric acid secretion. The study medication was administered in a double-blind fashion. An intravenous line was established.

All the patients received midazolam 2 mg intravenous on arrival to the operation room. The study medication was prepared by a person not involved with the perioperative or post-operative care. The medication consisted of 0.25 mg/kg of labetalol diluted with 0.9% saline up to 10 ml (Group B) and 0.5 mg/kg of esmolol diluted with 0.9% saline up to 10 ml (Group A). Anesthesia was induced with propofol 2 mg/kg and fentanyl given at 2 mcg/kg. Intubation was facilitated by rocuronium given at a dose of 1 mg/kg body weight. Intubation was done with an appropriately sized cuffed endotracheal tube. The duration to the onset of action of rocuronium was noted as the time for loss of all the twitch responses to a train of four stimulation. Patient taking more than 1 min from the time to laryngoscopy to intubation was eliminated from our study and not followed up. Patient lungs were mechanically ventilated with a mixture of oxygen:nitrous oxide at 1 L:2 L along with isoflurane to maintain an EtCO₂ of 4.5–5.0 kPa. After intubation, the monitoring was

done after 1 min, 3 min, 5 min, and 10 min. Monitoring was continued every 15 min till the completion of the surgery.

After the completion of surgery, the patients were monitored every 2 h till 24 h of the administration of the study drug. Any episodes of bradycardia were treated with atropine, and episodes of hypotension were treated with fluid boluses. The adverse reactions noted in the patients were nausea, vomiting, and dizziness.

Statistical analysis

The patient's demographic data including the American Society of Anesthesiologists physical status classification, history of post-operative nausea and vomiting or motion sickness, and the incidence of side effects were analyzed using Fisher's exact test. The demographic data including age and BMI and clinical data including intergroup variations were analyzed by unpaired Student's t-test. The clinical data showing intragroup variation were analyzed using paired Student's t-test. The time to onset of action of rocuronium was analyzed by Mann-Whitney U-test. A $p < 0.01$ was considered as statistically significant. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS™), Windows Versions 14.0, 15.0, and 16.0 (SPSS, Chicago, IL, USA).

RESULTS

The study was performed in the operating room of the ENT department in IMS and SUM Hospital, Bhubaneswar, India. 65 patients were screened and 60 patients were randomized and analyzed after surgery. The recruitment of the patients is depicted in the consort diagram (Fig. 1).

Distribution and duration of the surgical procedure were similar in the two groups as was the duration of surgery. The amount of propofol administered in the two groups was similar.

The labetalol and esmolol group both showed a decline in heart rate and systolic blood pressure after drug administration. The hemodynamic changes were similar during the extubation period. The onset of action of rocuronium was decreased by 11% in the labetalol group, and this difference was statistically significant.

The adverse reactions were more in labetalol group (Fig. 2). Dizziness was seen in 11 patients taking labetalol, and it was statistically significant. Other side effects were more in labetalol group but not statistically significant.

DISCUSSION

The noxious response to tracheal intubation produces a hemodynamic response which is not desirable in patients suffering from cardiac disorders. Various drugs are used to attenuate this response. In our study, we found out that labetalol which is a non-specific β blocker is as effective as esmolol in blunting of this response both during intubation as well as during extubation.

Rocuronium is an intermittent acting muscle relaxant. The unique ability of this drug compared to other intermittent acting muscle relaxant is its faster onset of action which is comparable with succinylcholine. The faster onset of action makes it suitable for use even in rapid sequence intubation [12,13]. The main drawback compared to succinylcholine is its much longer duration of action which restricts its use in a difficult airway scenario. A newly introduced drug called sugammadex [14,15] is a specific rocuronium antagonist, which reliably reverses the muscle relaxation produced by rocuronium given within minutes of rocuronium. This new drug now allows rocuronium to be reliable use in difficult airway scenario without worrying about the recovery of muscle power. Hence, rocuronium has the potential to replace succinylcholine [16], especially in those patients, it is not desirable to give succinylcholine which has an extensive list of its own side effects.

Esmolol has been very popular for attenuation of the hemodynamic response to tracheal intubation. It increases the onset of action of

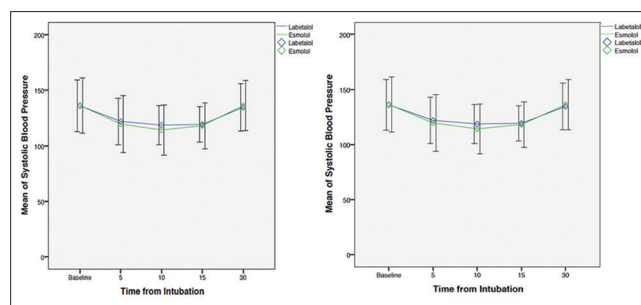


Fig. 1: Mean heart rate and mean blood pressure changes post intubation

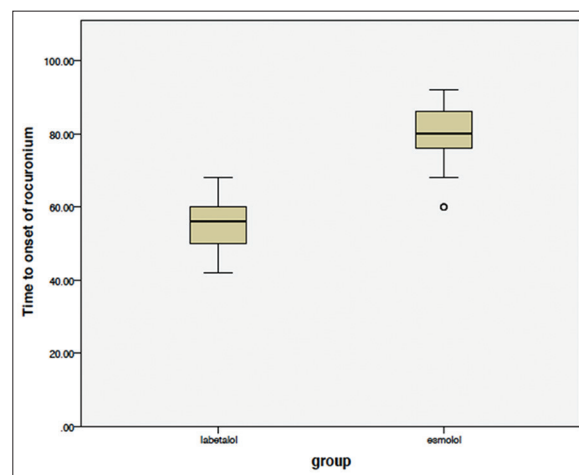


Fig. 2: Time to onset of action of rocuronium

rocuronium by as much as 26% [17,18]. It does this by predominantly decreasing the cardiac output. This may substantially increase the time to onset of action of rocuronium. This is not desirable in a rapid sequence intubation scenario where we want good relaxation and that too quickly. Lee *et al.* [19] have shown that nicardipine hastens the onset of action as compared to esmolol.

Labetalol a newer non-specific β antagonist is mainly used for the treatment of hypertension and congestive cardiac failure. It has got peripheral vasodilating property because of its α_1 antagonist property. In our study, labetalol reduced the time to onset of action of rocuronium, and this is mainly due to increased blood flow to the muscles. This helps to overcome the disadvantages of esmolol.

Labetalol also has a unique antioxidant property [20,21]. This may also help to decrease the stress response during surgery. The cost of labetalol is one-tenth that of esmolol. Thus, it has potential for use in difficult airway situations.

Further studies are required to establish the dosage and the role of labetalol in improving outcomes in difficult airway and head injury cases. The drawback of our study is the lack of any dose response. However, our main objective was to see whether labetalol is able to influence the time to onset of action of rocuronium or not. We can conclude that labetalol reduces the time to onset of action of rocuronium though further study is required to know the dose response of this drug for use as a premedication for anesthesia.

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